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600-1-081CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Ralph Steinman et al.	Examiner:	Ronald B. Schwadron
Serial No.:	09/586,704	Group Unit:	1644
Filed:	June 5, 2000		

For: IDENTIFICATION OF DEC, A RECEPTOR WITH C-TYPE LECTIN DOMAINS, NUCLEIC ACIDS ENCODING DEC, AND USES THEREOF

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Dated: March 15, 2007

Signature: Loretta Kavanagh
Loretta Kavanagh

RESPONSE TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The following remarks are responsive to a Notification of Non-Compliant Appeal Brief, mailed February 15, 2007 due for a response by March 15, 2007.

REMARKS

Applicants received a Notification of Non-Compliant Appeal Brief, mailed February 15, 2007, whereby it was noted that the Brief did not contain a statement of the status of all claims.

Applicants submit herewith a replacement Appeal Brief, which contains an amended SECTION III. STATUS OF THE CLAIMS, found on page 2 and request that this Appeal Brief replace the original as filed on December 21, 2006. Applicants assert that the status of all of the claims is now included in this section, and as such, corrects the deficiencies noted in the Notification of Non-Compliant Appeal Brief.

Fees

No fees are believed to be required for the present response, but if this is in error, the Commissioner is hereby authorized to charge any fees, or credit any overpayment, to Deposit Account No. 11-1153.

Respectfully submitted,

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Docket No.: 600-1-081CON
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Ralph Steinman *et al.*

Application No.: 09/586,704 Art Unit: 1644

Filed: June 5, 2000 Examiner: Ronald B. Schwadron

For: IDENTIFICATION OF DEC, A RECEPTOR WITH C-TYPE LECTIN DOMAINS, NUCLEIC ACID ENDODING DEC, AND USES THEREOF

MS Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

As indicated in the Notice of Appeal filed on June 28, 2006, Appellants hereby appeal the final decision of the Examiner in the above-identified application rejecting the subject matter of the pending claims. For the reasons set forth in this brief, Appellants respectfully request the Board of Patent Appeals and Interferences to reverse the Examiner's final rejection of the claimed subject matter. As Applicants are filing this Appeal Brief within the one month time period for response as noted in the Notification of Non-Compliant Appeal Brief, mailed on February 15, 2007, due for response on March 15, 2007, no fees are believed to be due. However, if this is in error, authorization is hereby given to charge any fees to deposit account number 11-1153.

I. REAL PARTY IN INTEREST

The real party in interest in the above-identified application is Rockefeller University, the assignee of the application.

II. RELATED APPEALS AND INTERFERENCES

A Notice of Appeal and related Pre-Appeal Brief Request for Review were filed on June 28, 2006 in a Continuation-in-Part application, U.S.S.N.: 09/925,284, having a filing date of August 9, 2001. No related interferences are known to Appellants, which will directly affect, or be directly affected by, or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 22-23, 26-30, and 35-45 are pending in this application. Claims 22-23 and 29-30 have been withdrawn from consideration. Claims 1-21, 24-25 and 31-34 have been canceled.

Claims 26-28 and 35-45 are on appeal and are set forth in the Claims Appendix (Appendix A).

IV. STATUS OF THE AMENDMENTS

A Notice of Appeal was filed June 28, 2006. All prior amendments have been entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Claims 26-28

The claims on appeal are drawn to a vaccine for inducing an immune response comprising an antigen conjugated to an anti-human DEC-205 antibody or an anti-murine DEC-205 antibody reactive with a human DEC-205 protein comprising the human DEC-205 protein as set forth in SEQ ID NO: 1. The amino acid sequence of SEQ ID NO: 1 corresponds to a partial (C-terminal) sequence of human DEC-205 (see, for example, page 3, lines 15-19; page 5, lines 13-23; page 7, lines 1-12; page 10, line 20 through page 11, line 14; page 55, line 30 through page 56, line 23; page 62, line 26 to page 63, line 15 and page 67, lines 15-21 of the specification as originally filed).

Claims 35-39

The claims on appeal are further drawn to a vaccine for inducing an immune response comprising an antigen conjugated to an anti-human DEC-205 antibody (claim 35) or an anti-mouse DEC-205 antibody (claim 36), wherein the antibody is reactive with the amino acid sequence as set forth in SEQ ID NO: 1. As noted above, the amino acid sequence of SEQ ID NO: 1 corresponds to a partial (C-terminal) sequence of human DEC-205 (see, for example, page 3, lines 15-19; page 5, lines 13-23; page 7, lines 1-12; page 10, line 20 through page 11, line 14; page 55, line 30 through page 56, line 23; page 62, line 26 to page 63, line 15 and page 67, lines 15-21 of the specification as originally filed).

Claims 40-45

The claims on appeal are also drawn to a vaccine for inducing an immune response comprising an antigen conjugated to an antibody which binds mouse DEC-205 having the amino acid sequence of SEQ ID NO: 3, wherein the antibody cross-reacts with human DEC-205. The amino acid sequence of SEQ ID NO: 3 corresponds to the full-length sequence of mouse DEC-205 (see, for example, page 5, lines 13-23; page 7, lines 1-12; page 10, line 20 through page 11, line 14; page 42, lines 24-31; page 55, line 30 through page 56, line 23; page 62, line 26 to page 63, line 15 and page 67, lines 15-21 of the specification as originally filed).

Please also see the Substitute Sequence Listing submitted in the present application on December 22, 2005, which identifies the full length mouse DEC-205 sequence as SEQ ID NO: 3.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellants present the following issue for review:

1. Whether claims 26-28 and 35-45 are properly rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

2. Whether claims 26-28 and 35-39 are properly rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

VII. ARGUMENTS

A. Summary of Examiner's Rejection of Claims 26-28 and 35-45 Under 35 U.S.C. § 112, First Paragraph, as Failing to Comply with the Written Description Requirement

The Examiner has rejected claims 26-28 and 35-45 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner asserts that the specification does not provide adequate written description for the claimed invention because, while the specification discloses the full length sequence of murine DEC-205 protein, it only discloses a partial sequence for human DEC-205. The Examiner asserts that, because human DEC-205 is approximately 1800 amino acids in length, the recitation in the claim of a 30 or 25 amino acid sequence derived from human DEC-205 does not provide adequate written description of a molecule that is almost 1800 amino acids in length. The Examiner further asserts that the claims encompass antibodies that bind any immunogenic epitope on the approximately 1775 undisclosed amino acids of DEC-205, and that the term human DEC-205 presumably encompasses full length human DEC-205 , as well as undescribed mutants and alleles of human DEC-205.

B. Appellants' Response

1. Each Independent Claim Requires Separate Consideration

Appellants respectfully disagree with the Examiner's rejection. As a preliminary matter, the scope of claims 26-28 and 35-45 varies and, as such, the assertions made by the Examiner are not equally applicable to all of these claims.

Specifically, contrary to the Examiner's opinion that the claimed antibody conjugates do not bind to any specific epitope of human DEC-205, claims 35-39 are drawn to antibody conjugates which do, indeed, bind to a particular epitope of human DEC-205, namely the C-terminal sequence (SEQ ID NO: 1).

Similarly, that the present specification teaches a partial human DEC-205 sequence is also irrelevant with respect to claims 40-45, since these claims are drawn to a vaccine comprising an antigen conjugated to an antibody that binds to *full length murine DEC-205 protein* (SEQ ID NO: 3). Thus, the Examiner's statement that the antibody conjugates of claims 40-45 bind to "undisclosed amino acids of DEC 205" is incorrect. Indeed, the full length sequence of murine DEC 205 is explicitly provided in

the present application as SEQ ID NO: 3. Moreover, while the antibody conjugates of claims 40-45 also cross-react with human DEC-205, the epitopes of human DEC-205 that the conjugates bind to are thus, by definition, shared with (*i.e.*, cross-reactive with) murine DEC-205. As such, the sequence of these epitopes is provided as part of the full length murine DEC-205 sequence recited in the claims (SEQ ID NO: 3).

For at least the reasons above, the reasons provided by the Examiner for rejecting claims 35-45 as lacking written description under 35 U.S.C. §112, first paragraph, do not apply or support the rejection.

Finally, with respect to claims 26-28, drawn to a vaccine comprising an antigen conjugated to an antibody that binds to human DEC-205 protein comprising the partial amino acid sequence of SEQ ID NO: 1, Appellants respectfully submit that while Appellants' specification does not recite the full length human DEC-205 sequence, or the sequence of each and every variant of human DEC-205, this does not *de facto* mean that the pending claims fail to comply with the written description requirement. Importantly, it is well-established that the written description standard is not a bright line test, but instead takes into consideration a number of different factors. As discussed in detail below, Appellants' disclosure of the partial human DEC-205 sequence and the full length murine DEC-205 sequence, in combination with knowledge available in the art, were sufficient to demonstrate to one of ordinary skill that they had full possession of the complete human DEC-205 protein, and antibody conjugates against the protein, at the time the present application was filed.

2. The Descriptive Text Needed to Satisfy the Written Description Standard Must be Considered in Relation to the Scientific Knowledge in Existence at the time of the Invention, the Skill in the Art, and Correlation of a Disclosed Function to a Known Structure

The mere fact that Appellants' specification does not recite the full length human DEC-205 sequence does not alone mean that any of the claims on appeal fail to comply with the written description requirement.

Moreover, Appellants respectfully disagree with the Examiner's assertion that the decision in *Capon v. Eshhar* (418 F.3d 1349, 1357 (Fed. Cir. 2005)) "is not relevant to the claims under consideration." While the claims on appeal may differ from the claims on appeal in *Capon v. Eshhar*, the Court took considerable effort to lay out the underlying framework for determining written description in other cases moving

forward, and to clarify that written description, like enablement, must be determined on a case by case basis. Specifically, the standard for meeting the written description requirement and showing possession of the claimed invention, as articulated by *Capon v. Eshhar*, differs for every patent specification depending upon a number of factors, including the scientific knowledge in existence at the time of the invention, the skill in the art, the predictability of the claimed subject matter, and correlation of a described function to a known structure. Again, Appellants do not argue that the claims at issue in *Capon v. Eshhar* were the same as in the present case, rather that the written description standard articulated by the Court, when applied in the present case, is fully satisfied.

Specifically, as discussed further below, the maturity of the science and skill in the art at the filing date of the present invention were such that one of ordinary skill could predictably obtain full-length proteins, such as DEC-205, based on partial sequences, as well as predictably obtain antibodies against the full-length protein (or any region or variants of the protein). As such, Appellants teachings in the specification, combined with the knowledge available in the art, demonstrate that Appellants were in full possession of the presently claimed invention at the time of filing.

3. Isolation and Cloning of Proteins, and Generation of Antibodies Were Highly Mature Technologies at the Time of the Present Invention

Indeed, at the filing date of the present application (*i.e.*, in 1995), technologies for isolating, characterizing and cloning proteins were highly developed, as were technologies for generating antibodies against such proteins. For example, several well known techniques were available for cloning proteins, including human DEC-205, based on a given partial amino acid sequence of the protein (see, for example, page 20, line 30 through page 21, lines 1-19; as well as page 25, lines 25-31 through page 31, lines 1-16 of the present application). Additionally, techniques for expressing cloned proteins (see, for example, page 31, lines 18-31 through page 35, lines 1-30 of the present application) and for generating antibodies against the proteins were equally well known (see, for example, page 42, lines 23-31 through page 45, lines 1-19, and particularly page 42, lines 28-31 in the present application). Once armed with a partial amino acid (*i.e.*, a peptide derived from a given protein), it was also well within the

skill of the art to use these techniques to generate antibodies against such peptides and to isolate the full-length protein from its natural source.

Appellants specifically illustrated this in relation to mouse DEC-205. In particular, Appellants successfully isolated and characterize full-length mouse DEC-205 from whole murine thymus using mAb NLDC-145, an anti-mouse DEC-205 antibody (see page 63 of the present application). Additionally, Appellants successfully raised antibodies against N-terminal peptides from mouse DEC-205 protein (see, for example, page 62, lines 26-32 and page 63, lines 1-15 of the present application). This provides ***clear evidence*** that the partial human DEC-205 sequence described in the present disclosure put Appellants in possession of the complete DEC-205 protein and antibodies against the protein.

Additionally, in the present application, Appellants teach a partial (C-terminal) sequence (SEQ ID NO: 1) of human DEC-205 protein. Appellants further teach the highly homologous full-length sequence of mouse DEC-205 protein (SEQ ID NO: 3), along with an in-depth characterization of this protein (including its ability to deliver antigen to an active antigen processing compartment of dendritic cells). Appellants also describe well-known techniques for cloning proteins (including human DEC-205) based on a given partial amino acid sequence of the protein, expressing cloned proteins and generating antibodies against the proteins. Based on these teachings, it was well within the skill of the art to have generated anti-DEC-205 antibodies. It was also well within the skill in the art to have generated full-length human DEC-205 protein, as well as variants of the human DEC-205 protein.

In fact, as evidenced by the Declaration by Dr. Michel Nussenzweig (Appendix B) and related publications submitted with Appellants' Amendment and Response dated January 3, 2005, the cloning techniques and techniques for generating antibodies described in the specification were ultimately successfully used to clone and isolate human DEC-205 and to produce antibodies against full-length human DEC-205. This provides clear evidence that Appellants were in fact indeed in possession of the claimed invention based on the descriptive text provided within the four corners of Appellants' originally filed disclosure.

4. The Structure and Function of Human DEC-205 Correlates to the Structure and Function of Mouse DEC-205 Protein

Finally, the Written Description requirement may be satisfied if the disclosed function of the claimed invention sufficiently correlates to a particular, known structure. In the present case, the structure and function of human DEC-205 clearly correlates to that of mouse DEC-205, the characteristics of which (including full-length sequence) are described in detail in the present disclosure. Accordingly, the fact that Appellants provide an in-depth characterization of mouse DEC-205, including its full-length sequence, which correlates to human DEC-205, provides further basis for fully meeting the Written Description requirement.

In sum, the teachings set forth in Appellants' specification, in combination with the high level of skill and knowledge in the art at the time of the invention, and the proven predictability of the technologies involved in the invention, clearly satisfies the standard for Written Description according to the guidelines articulated by the CAFC in *Capon v. Eshhar* (CAFC 2005), and demonstrates possession of the claimed invention.

C. Summary of Examiner's Rejection of Claims 26-28 and 35-39 Under 35 U.S.C. § 112, First Paragraph, as Failing to Comply with the Written Description Requirement

The Examiner has rejected claims 26-28 and 35-39 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner alleges that there is no support in the specification for a human DEC-205 protein comprising an amino acid sequence as set forth in SEQ ID NO: 1. The Examiner further asserts that, although the specification teaches that SEQ ID NO: 1 is a peptide derived from DEC-205, there is no support for a DEC-205 protein comprising the peptide wherein the molecule could have any amino acids in association with the aforementioned sequences recited in the claim.

D. Appellants' Response

As an initial point, it is unclear to Appellants, based on the Examiner's comments, what the distinction is between the former 35 U.S.C. § 112, first paragraph, rejection of claims 26-28 and 35-45, and the present § 112, first paragraph, rejection of claims 26-28 and 35-39. Indeed, both rejections appear to be based on the same

premise, *i.e*, that the claims lack written description because the specification teaches a partial human DEC 205 sequence. Appellants note, however, that the former rejection has been applied to claims 26-28 and 35-45, whereas the present rejection has been applied only to claims 26-28 and 35-39.

Accordingly, with respect to claims 35-39, Appellants again respectfully note that these claims are drawn to a vaccine that employs antibody conjugates defined as binding to a *particular* epitope on human DEC 205, the sequence of which is explicitly taught in the application (SEQ ID NO: 1, not SEQ ID NO: 7, as noted by the Examiner). Therefore, the Examiner's assertion that the specification fails to provide support for a human DEC 205 protein comprising the partial sequence of SEQ ID NO: 1 does not provide a basis for rejecting claims 35-39 for lack of written description.

Moreover, for the many reasons discussed above in Section B, Appellants respectfully submit that the specification does indeed provide full support for a human DEC 205 protein comprising SEQ ID NO: 1, as recited in claims 26-28. Again, the mere fact that the disclosure teaches partial sequences for human DEC 205 does not alone mean that the claims covering antibody conjugates which bind to human DEC 205 comprising such sequences lack written description. Whether claims 26-28 comply with § 112, first paragraph, depends on a variety of factors, as discussed above in relation to the previous rejection (Section B). When applied in the present case, given the teachings in Appellants' specification, in combination with the skill and knowledge available in the art at the time the present application was filed, clearly demonstrate that Appellants possessed the complete human DEC-205 protein recited in claims 26-28.

As previously discussed in detail, Appellants teach the partial C-terminal sequence of human DEC-205 (SEQ ID NO: 1). Based on this partial amino acid sequence, it was well within the skill of the art to have used known techniques to generate antibodies against this peptide, and to have predictably isolated the full-length protein or variants from its natural source. In fact, the maturity of the science and skill in the art at the time of the present invention were such that those of ordinary skill in the art were routinely obtaining full-length proteins based on partial sequences, as well as predictably obtaining antibodies against such full-length proteins. This is specifically attested to in the Declaration submitted by Declaration by Dr. Michel Nussenzweig (Appendix B). Further, the fact that Appellants provide an in-depth characterization of mouse DEC-205, including its full-length sequence, which

correlates to human DEC-205, provides further basis for fully meeting the Written Description requirement.

In sum, for at least the foregoing reasons, claims 26-28 and 35-39 fully comply with 35 U.S.C. § 112, first paragraph.

VIII. CONCLUSION

Appellants submit that claims 26-28 and 35-45 comply with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the Board reverse the rejection of claims 26-28 and 35-45 for the reasons set forth above.

Dated: 3/15/07

Respectfully submitted,

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CLAIMS APPENDIX A

26. (Previously presented) A vaccine for inducing an immune response comprising an antigen conjugated to an anti-human Dendritic and Epithelial Cell 205 (DEC-205) antibody or an anti-murine DEC-205 antibody reactive with a human DEC-205 protein, said human DEC-205 protein comprising an amino acid sequence as set forth in SEQ ID 1.

27. (Previously presented) The vaccine of claim 26, wherein the antigen is selected from the group consisting of a virus, a bacterium, a parasite, and a tumor.

28. (Original) The vaccine of claim 26, wherein the immune stimulator is selected from the group consisting of a cytokine, a lymphokine, and an adjuvant.

35. (Previously Presented) A vaccine for inducing an immune response comprising an antigen conjugated to an anti-human Dendritic and Epithelial Cell 205 (DEC-205) antibody, wherein the antibody is reactive with the amino acid sequence as set forth in SEQ ID NO: 1.

36. (Previously Presented) A vaccine for inducing an immune response comprising an antigen conjugated to an anti-mouse Dendritic and Epithelial Cell-205 (DEC-205) antibody, wherein the antibody is reactive with the amino acid sequence as set forth in SEQ ID NO: 1.

37. (Previously Presented) The vaccine of any one of claims 26, 35, or 36, further comprising an immune stimulator.

38. (Previously Presented) The vaccine of claim 37, wherein the immune stimulator is selected from the group consisting of a cytokine, a lymphokine, and an adjuvant.

39. (Previously Presented) The vaccine of any one of claims 26, 35, or 36, wherein the antigen is selected from the group consisting of a virus, a bacterium, a parasite, and a tumor.

40. (New) A vaccine for inducing an immune response comprising an antigen conjugated to an antibody which binds mouse Dendritic and Epithelial Cell 205 (DEC-205) having the amino acid sequence of SEQ ID NO: 3 , wherein the antibody cross reacts with human DEC-205.

41. (New) The vaccine of claim 40, further comprising an immune stimulator.

42. (New) The vaccine of claim 41, wherein the immune stimulator is selected from the group consisting of a cytokine, a lymphokine, and an adjuvant.

43. (New) The vaccine of claim 40, wherein the antigen is selected from the group consisting of a virus, a bacterium, a parasite, and a tumor antigen.

44. (New) The method of claim 40, wherein the antigen is bound to the antibody to DEC-205 by means of a cross-linking agent.

45. (New) The method of claim 40, wherein a light chain or a heavy chain of the antibody to DEC-205, and the antigen, are present on a single polypeptide chain.

EVIDENCE APPENDIX

Appendix B is a copy of the Declaration by Dr. Michel Nussenzweig, originally submitted with the Amendment and Response filed by Appellants dated January 3, 2005.

Appendix C is a copy of Guo *et al.*, *Hum Immunol.* 2000 Aug; 61(8):729-38, which was cited in the Declaration by Dr. Michel Nussenzweig that was submitted with the Amendment and Response filed by Appellants on January 3, 2005.

RELATED PROCEEDINGS APPENDIX

Please note that a Pre-Appeal Brief Request for Review and related Appeal have been filed in the Continuation-in-Part application, U.S.S.N.: 09/925,284 (filed August 9, 2001). A Notice of Panel Decision from the Pre-Appeal Brief Review issued on August 8, 2006 and an Appeal Brief was filed on November 27, 2006 with a Petition for a three month extension of time.